Asymmetric Synthesis of Secondary and Tertiary Propargylic Alcohols by Umpolung of Acetylenic Sulfones and *Ortho*-Sulfinyl Carbanions

Ricardo I. Rodríguez,[†] Elsie Ramírez,[†] Francisco Yuste,[†,*] Rubén Sánchez-Obregón[†] and José Alemán[‡,§,*]

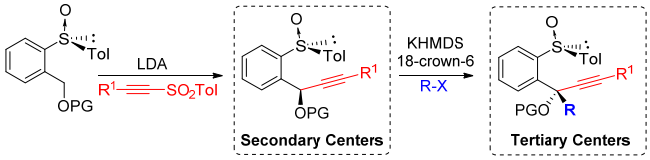
[†] Instituto de Química, Universidad Nacional Autónoma de México, Circuito Exterior, Cd. Universitaria, Coyoacán 04510, México City, México

[‡] Departamento de Química Orgánica (módulo-1), Universidad Autónoma de Madrid, Cantoblanco, 28049-Madrid, Spain

[§] Institute for Advanced Research in Chemical Sciences (IAdChem), Universidad Autónoma de Madrid, 28049, Madrid, Spain

KEYWORDS. Organolithium, sulfoxides, alkynes, umpolung, asymmetric synthesis.

ABSTRACT: The generation of diasteromerically enriched secondary benzyl propargyl alcohols by the asymmetric addition of *ortho*-sulfinylbenzyl carbanions to sulfonylacetylene derivatives via formation of Csp-Csp^3 bond is described. This reaction proceeds through an unusual α-attack (*anti*-Michael addition) of the *ortho*-sulfinylbenzyl carbanions, followed by elimination of the arylsulfonyl moiety. The scope of this alkynylation reaction is also discussed. Moreover, the development of a new approach for the synthesis of optically active tertiary benzylpropargyl alcohols is described, discussing the possible stereocourse of the reaction so as the influence of the ether 18-crown-6 and steric importance of acetylenic substituent.



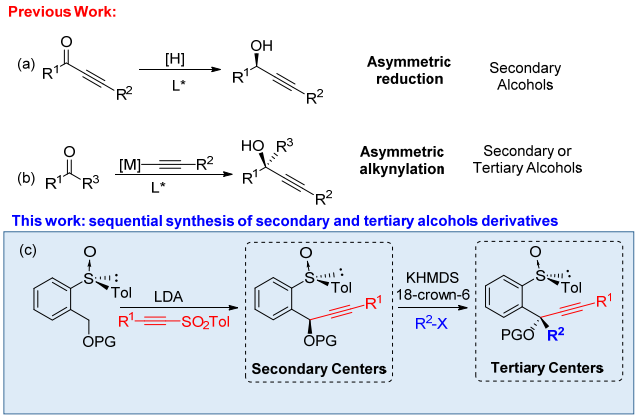
INTRODUCTION

The asymmetric synthesis of secondary and tertiary alcohols continues to be of considerable interest. The importance thereof stems from their ubiquitous presence in natural products, pharmaceutical agents, and other biologically active compounds.[1] In addition, secondary and tertiary alcohols are important substrates for a large number of subsequent transformations[2] and starting materials for the synthesis of natural products.[3]

Several research groups have described the addition of diverse organometallic species to acetylenic aldehydes and ketones in the presence of asymmetric ligands, leading to enantiomerically enriched secondary and tertiary alcohols (equations a and b, Scheme 1). Two main approaches have been described for the synthesis of these important propargylic alcohols. One route thereto involves the enantioselective reduction of the carbonyl moiety (equation a). Unfortunately, this synthesis is unpractical because of the limited accessibility and stability of the alkynyl ketones (very reactive Michael acceptors).[4] A more useful approach involves the enantioselective addition of alkyl acetylide anions to aldehydic or ketonic carbonyl groups[5] (equation b, Scheme 1). A large number of catalytic systems have been developed for this addition reaction, including alkynyl zinc reagents, among others. Unfortunately, this approach is often associated with high catalyst loadings, long reaction times, and large reagent excesses.[6] Most of these methods also require the use of transition metals for the formation of the Csp-Csp^3 bond, which is often considered to be a handicap by pharmaceutical companies, especially for large-scale syntheses.[7]

In 2012, we reported that organolithium reagents underwent an unexpected addition to the carbon atom alpha to the sulfonyl moiety of arylsulfonylacetylenes (anti-Michael addition) with subsequent beta elimination of lithium arylsulfinate to generate disubstituted acetylenes.[8] This transition metal free process occurred with both alkyl and aryl lithium reagents. The purpose of this work is to describe the extension of this methodology to the synthesis of secondary and tertiary propargylic alcohols beginning

with the carbanion derived from the optically pure protected *o*-(*p*-tolylsulfinyl)benzyl alcohols[9] shown in equation c, Scheme 1. In addition, we describe conditions for removal of the alcohol protecting group as well as the tolylsulfinyl moiety from some of the products.



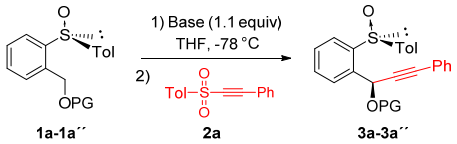
Scheme 1. Previous work and present work described in this communication (PG = protecting group).

RESULTS AND DISCUSSION

Our studies started with optically pure (*S*)-2-*p*-tolylsulfinyl benzyl alcohol in which the hydroxyl moiety was masked with various protecting groups (**1a-1a´´**, Table 1). The benzylic anions derived therefrom with various bases were reacted with phenyl-*p*-tolylsufonylacetylene **2a** in tetrahydrofuran at −78 °C. The data presented in Table 1 showed that the methoxymethyl (MOM) protecting group gave the most desirable result in terms of product yield and diastereoisomeric ratio, but only using LDA as deprotonating base (entry 1). The methyl and the TBDMS showed good reactivity, but the observed diastereomeric ratio was moderated (**3a**' and **3a**", entries 2 and 3). Interestingly, metalation of the MOM protected compound **1a** with lithium or potassium hexamethyldisilazide did not generate the desired product, probably because of metalation of **1a** failed to occur.[10]

The lithiated compound **1a**, generated under the optimized conditions shown in Table 1, was then reacted with various arylsulfonylacetylenes **2a-h** (Table 2). The reaction was successful for different aromatic groups, with electron-withdrawing groups such as 3,5-bis(trifluoromethyl), and 4-Cl (entries 2 and 3) and with electron donating groups such as 4-CH_3O (entry 4). The use of heterocycles, such as the thienyl group, was also compatible (entry 5), and the use of bulkier aromatic groups like naphthyl afforded alkyne **3f** with good yield and diastereoselectivity (entry 6). When the reaction was carried out with acetylenes containing an alkyl chain (entry 7), only starting material was found, maybe due to the competitive deprotonation of the propargylic position.[11] The result with the TIPS-sulfone **2h** is noteworthy in terms of both chemical and optical yield because of the expected facile removal of this moiety and easy transformation to alkyl-alkyne derivatives.

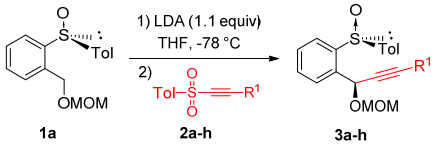
Table 1. Screening of different protecting groups for the alkynylation process.[a]



Entry	PG	Base	d.r.[b]	Yield (%)[c]
1	MOM	LDA	>98:<2	68-**3a**
2	Me	LDA	66:33	45-**3a´**
3	TBDMS	LDA	91:9	60-**3a´´**
4	MOM	KHMDS	--	--
5	MOM	LHMDS	--	--

[a] All reactions were performed on a 0.1 mmol scale in 4 mL of THF and stopped after 1 h. [b] Determined by H-NMR. [c] Yields of pure major diastereomer after flash chromatography. PG = protecting group.

Table 2. Scope in the synthesis of secondary alcohol derivatives 3.[a]

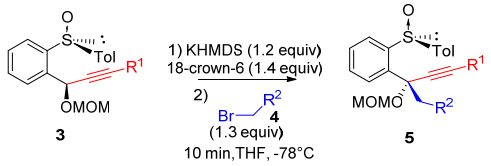


Entry	2 (R^1)	d.r.[b]	Yield (%)[c]
1	Ph	>98:<2	68-**3a**
2	3,5-$(CF_3)_2$-C_6H_3	92:8	62-**3b**
3	4-Cl-C_6H_4	92:8	45-**3c**
4	4-CH_3O-C_6H_4	96:4	68-**3d**
5	3-Thienyl	>98:<2	50-**3e**
6	1-Naphthyl	97:3	60-**3f**
7	*n*-Bu	n.r.	-
8	TIPS	>98:<2	65-**3h**

[a] All reactions were performed on a 2.73 mmol scale in 10 mL of THF and stopped after 1 h. [b] Determined by H-NMR. [c] Yields of pure major diastereomer after flash chromatography.

Given the increased acidity of the benzylic hydrogen of the alkynylated compounds **3** compared with **1**, we studied the alkylation of **3a** with benzyl bromide after deprotonation with strong bases (Table 3), giving access to tertiary centers.[12] The use of LDA as the base did indeed generate the corresponding product mixture with modest efficiency and diastereoselectivity (entry 1). This alkylation reaction was not successful when LHMDS was used as base. However, KHMDS was especially efficient in terms of yield and diastereoselectivity in the presence of 18-crown-6 as an additive (entry 2). These conditions were then utilized for the remaining procedures shown in Table 3. The reaction allowed usage of different groups at the alkylating reagents. Therefore, methoxy group at the benzyl reagent (**4b**) gave tertiary center **5b** with excellent yield and good diastereoisomeric ratio (entry 3). The use of a *p*-nitrile group at the benzyl reagent (**4c**) allowed the synthesis of **5c** with a completed chemoselectivity (CN vs $ArCH_2Br$) and good diastereoselectivity (entry 4). Other propargylic starting materials **3** were used, allowing the synthesis of the *p*-methoxybenzyl group (**5d**) with moderate selectivity (entry 5).

Table 3. Scope in the synthesis of tertiary alcohol derivatives **5**.[a]

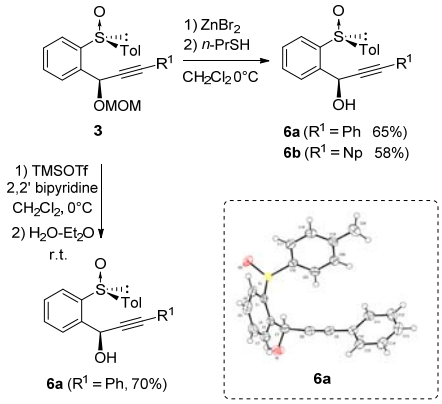


Entry	3 (R^1)	4 (R^2)	d.r.[b]	Yield (%)[c]
1[d]	Ph	Ph	60:40	25-**5a/5a´**
2	Ph	Ph	80:20	56-**5a/5a´**
3	Ph	*m*-MeO-C_6H_4	80:20	68-**5b/5b´**
4	Ph	*p*-CN-C_6H_4	86:14	71-**5c/5c´**
5	*p*-MeO-C_6H_4	Ph	70:30	50-**5d/5d´**
6	TIPS	*m*-MeO-C_6H_4	>98:<2	51-**5e**
7	Ph	-CC-CH_3	55:45	52-**5f/5f´**[e]
8	Ph	$CH=CH_2$	70:30	64-**5g/5g´**[e]
9[f]	Ph	H	80:20	56-**5h/5h´**
10	TIPS	-CC-CH_3	91:9	66-**5i/5i´**

[a] All reactions were performed on a 0.1 mmol scale in 4 mL of THF and stopped after 1 h. [b] Determined by H-NMR. [c] Yields of pure major diastereomer after flash chromatography [d] In this case, LDA was used as a base. [e] Yields of inseparable diastereomeric mixture after flash chromatography [f] This reaction was carried out without 18-crown-6 and with MeI as electrophile.

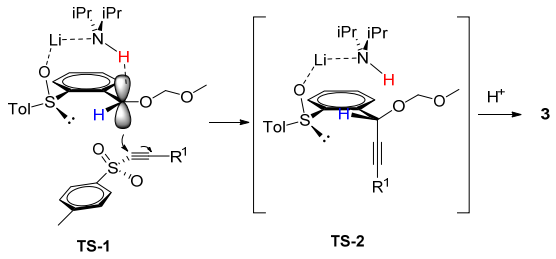
The exceptional diastereoselectivity observed for the alkylation of TIPS substituted **3h** with *m*-methoxybenzyl bromide is noteworthy (entry 6). The use of other electrophiles like propargyl and allyl bromides, allowed the synthesis of 1,5 diyne **5f** and 1,5 enyne **5g,** respectively (entries 7 and 8) with moderate diastereoselectivity. In addition, the alkylation reaction with methyl iodide (entry 9) is of considerable interest and significance, because of the existence of previous evidence reporting failure on this kind of reaction.[8d] When **3h** underwent the alkylation reaction with 1-bromo-2-butyne as electrophile, the diastereoselectivy dramatically increased from 55:45 to 91:9 (compare entries 7 and 10, Table 3).

Aiming to obtain secondary benzylpropargyl alcohols, we proceeded to remove the protecting group. Classic cleavage of MOM group involves strong acidic conditions, however, being a secondary benzylpropargyl alcohol, the possibility to undergo an elimination reaction through loss of water was very high.[13] Two methodologies under mild conditions were successfully used,[14] in both cases the reaction proceeded with good yields. The absolute configuration of compounds **3** were determined by X-ray analysis of a crystal of **6a** (bottom-right, Scheme 2) and for the rest of compounds **3** we assumed the same stereochemical outcome (*SS*, *1R*).[15]



Scheme 2. Deprotection of secondary alcohols 6 and ORTEP view of 6a (ellipsoids shown at the 50% probability level).

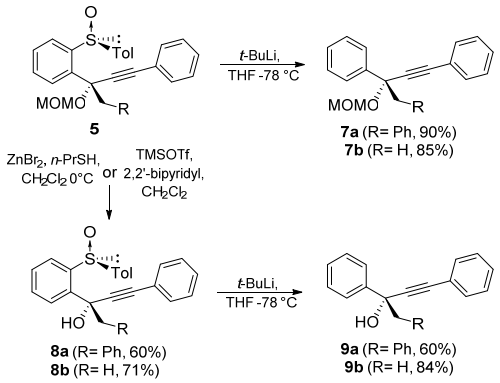
Our group has previously explained the stereochemical results obtained in these reactions.[9] The carbanion of **TS-1** would result in the deprotonation of compound **1**, using LDA as base, which has previously associated to the sulfinyl oxygen. According to the theoretical calculations,[9c] the benzylcarbanion just formed should adopt the structure of **TS-1** (Scheme 3), stabilized by a hydrogen bond formed with the nitrogen of the iPr_2NH, which also acts as a ligand of the lithium cation. Then, the approach of the sulfone to the *re* face, being the *si* face hindered by the amine system, (**TS-2**) would result in the formation of diastereoisomers **3**, with *R* configuration at the propargylic carbon.



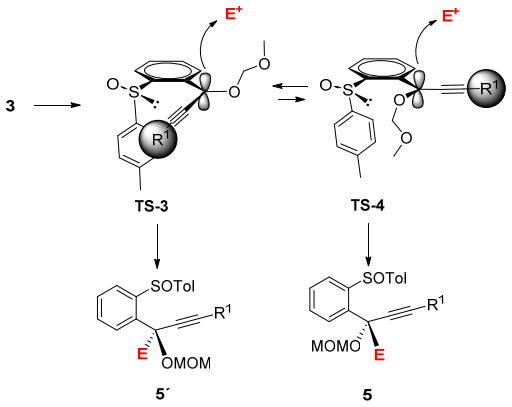
Scheme 3. Proposed mechanism for the monoalkylation of 1.

We then focused our attention in transformations on tertiary alcohol derivatives **5**. Desulfinylated compounds **7a** and **7b** were obtained under smooth conditions by reaction with *t*-BuLi (top Scheme 4). As one of our final goals, we performed the cleavage of the MOM group to get the tertiary benzylpropargyl alcohols **8** and **9** (bottom, Scheme 4). Therefore, compounds **5a** and **5b** were deprotected under standard conditions to produce **8a** and **8b**, followed by treatment with *t*-BuLi, rendering the desulfinated products **9a** and **9b** in good yields. The absolute configuration of major diastereoisomers **5** was obtained by comparison of optical rotation values of **8b** and **9b** with those reported in the literature,[6,16] establishing as (*Ss,S*) and (*R*), respectively (see experimental section for further details). Taking into account the similarities in ^{1}H and ^{13}C NMR chemical shifts and optical rotation values of compounds **5**, we assumed a similar stereochemical outcome for all tertiary alcohols.

Scheme 4. Desulfinylation and deprotection of tertiary alcohols derivatives 5.



The results obtained in the synthesis of tertiary alcohols derivatives **5** are similar to those reported for the alkylation reactions of similar carbanions,[17] which suggests a similar stereocourse. This result is not compatible with the control by chelation model as it was in **TS-1** and **TS-2** (see Scheme 3), which is in this latter case in the presence of crown ether. The naked carbanion formed with KHMDS/18-crown-6 ether (K should be sequestered by the crown ether) will adopt the planar sp^2 structures **TS-3** and **TS-4** depicted in Scheme 5. The sulfinyl group adopts an *anti*-arrangement with respect to the carbanionic carbon, adopting the most stable conformation form from the electrostatic point of view. Whereas the conformation towards the carbanionic carbon must be controlled by steric ground, where the lone electron pair may interact either with the triple bond (**TS-3**) or with the methoxymethyl group (**TS-4**). The approach of the electrophile from the upper face of carbanion **TS-3** and **TS-4**, is clearly favored because its steric interactions with the *p*-tolyl group are avoided. The delicate steric balance between **TS-3** and **TS-4** (SOTol/CC-R^1 vs SOTol/MOM) induces a significant change in the final observed stereochemistry. Therefore, when a phenyl ring was tested as substituent of the triple bond (entries 2-4, Table 3), there were found diastereoselectivity values near to 80:20. However, when a bulkier group, such as TIPS (entries 6 and 10) was used, the higher interaction between the triple bond and the sulfinyl moiety, causes an equilibria displacement to the intermediate conformer **TS-4**, increasing diastereoselectivity (entries 6, d.r. >98:<2 and 10, d.r. 91:9).



Scheme 5. Proposed mechanism for the monoalkylation of 3.

CONCLUSIONS

In conclusion, we demonstrated that an umpolung between an *ortho*-sulfinylated benzyl carbanion as nucleophile and an arylsulfonylacetylene as electrophile, represents an attractive approach for the generation of diastereomerically pure secondary benzyl propargyl alcohols. Moreover, we have taken advantage of the great stability of the sp^2 benzylpropargyl carbanion generated, allowing us to introduce in a stereocontrolled procedure allyl, benzyl and propargyl moieties in moderate and good yields. This is a transition metal-free procedure, and the wide range of electrophiles that can be used, represent the possibility of synthesizing compounds that are potential pharmaceutical intermediates. Also, a rational explanation for the stereochemical results of the reactions based on the obtained data was presented.

EXPERIMENTAL SECTION

General considerations: All moisture-sensitive reactions were carried out in flame-wired glassware equipped with rubber septa under a positive pressure of argon and monitored by TLC. Flash chromatography was performed with silica-gel 60 (230-

400 mesh ASTM). Melting points were determined in open capillary tubes and are uncorrected. The optical rotations were measured at room temperature (concentration in g/100 mL). The NMR spectra were acquired in $CDCl_3$ solutions at 300 and 75 MHz for ^1H and ^{13}C NMR, respectively. J values are given in hertz. The diastereomeric excesses were determined by 300 MHz ^1H NMR spectroscopy. The mass spectra were obtained on a JEOL-JMS-T100LC and JEOL-JMS-700 apparatus. All described compounds were over 97% pure by NMR analysis.

(*S*)-1-((Methoxymethoxy)methyl)-2-(*p*-tolylsulfinyl)benzene 1a.

Method A: To a stirred solution of (*S*)-(2-(*p*-tolylsulfinyl)phenyl)methanol **1**[18] (500 mg, 1.64 mmol, 1 equiv) in dry dichloromethane (20 mL) at 0 ºC, DIPEA (0.88 mL, 4.92 mmol, 3 equiv), NaI (50 mg, 0.328 mmol, 0.2 equiv) and MOMCl (0.186 mL, 2.46 mmol, 1.5 equiv) were added successively. The resulting mixture was stirred at rt for 10 h. Then, a saturated solution of $NaHCO_3$ (15 mL) was added and the reaction was neutralized with a solution of 10% AcOH (10 mL). The organic phase was dried (Na_2SO_4) and concentrated. The residue was purified by flash column chromatography using EtOAc/hexane 1:4 as eluent to produce **1a** as a colorless oil (483 mg, 82%).

Method B: To a stirred solution of 1-bromo-2-[(methoxymethoxy)methyl]benzene (2.2 g, 9.52 mmol, 1.1 equiv) in THF (200 ml) at -78 ºC under argon atmosphere, was added a solution 2M in hexanes of *n*-BuLi (4.76 mL, 9.52 mmol, 1.1 equiv). After 40 min, a solution of (*S*)-menthyl sulfinate (2.54 g, 8.65 mmol, 1 equiv) in THF (50 mL) was added via cannula. When the reaction was completed (30 min), the mixture was hydrolyzed with saturated aqueous NH_4Cl (20 mL) at -78 ºC and extracted with CH_2Cl_2 (3 x 50 mL). The organic layer was washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography eluting with EtOAc/hexane 3:7 to produce **1a** (61%).

Prepared through method A. $[\alpha]_D^{20}$ -175 (*c* 0.5, acetone); ^1H $[\alpha]_D^{20}$ -114.7 (*c* 4.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.95 (dt, *J* 7.1 and 1.3 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.43 (dd, *J* 4.3 and 1.4 Hz, 3H), 7.25 – 7.18 (m, 2H), 4.70 (d, *J* 5.9 Hz, 2H), 4.65 (d, *J* 1.8 Hz, 2H), 3.37 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.9, 141.6, 141.0, 135.6, 130.8, 129.6, 128.9, 125.3, 125.3, 125.0, 95.6, 65.4, 55.4, 21.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{16}H_{19}O_3S$ 291.1054; Found 291.1054.

General Procedure for the Alkynylation Reactions.

Over a solution of LDA previously prepared from *n*-BuLi (2M in hexanes, 1.2 equiv) and diisopropylamine (2.2 equiv) in THF (10 mL) at -78 ºC, a solution of sulfoxide **1a** (1 equiv) in THF (10 mL) was added. After 20 min, a solution of corresponding sulfone **2** (1.1 equiv) in THF (10 mL) was added via cannula. When the reaction was complete (TLC), a saturated aqueous NH_4Cl (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The organic extract was washed with brine, dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography using as eluent a mixture of EtOAc/hexane as indicate in each case, to produce **3**.

***(R,S_S)*-1-(1-(Methoxymethoxy)-3-phenylprop-2-ynyl)-2-(*p*-tolylsulfinyl)benzene 3a**. The product was obtained as single diasteromer following the standard procedure from **1a** (200 mg, 0.69 mmol) and sulfone **2a**[19] and was purified by flash column chromatography using a mixture of EtOAc/hexane 5:95 as eluent. Yellow oil (183 mg, 68% yield, d.r. >98:<2).

$[\alpha]_D^{20}$ -190.8 (*c* 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.03-7.96 (m, 1H), 7.78-7.72 (m, 1H), 7.60-7.49 (m, 4H), 7.36-7.23 (m, 5H), 7.18 (d, *J* 8.3 Hz, 2H), 6.04 (s, 1H), 5.09 and 4.69 (AB system, 2H), 3.46 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.6, 142.3, 141.5, 137.2, 131.9, 131.6, 130.1, 130.0 128.9, 128.4, 128.3, 125.8, 125.3, 122.1, 94.1, 88.2, 85.9, 63.7, 56.3, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{23}O_3S$ 391.1368; Found 391.1379.

***(R,S_S)*-1-(3-(Methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)prop-1-ynyl)-3,5-bis(trifluoromethyl)benzene 3b.** The product was obtained as single diastereomer following the standard procedure from **1a** (180 mg, 0.62 mmol) and sulfone **2b**[8b] and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 5:95 as eluent. Colorless oil (202 mg, 62% yield, d.r. 98:2). This product is photo sensible and must be kept in the dark.

^1H NMR (300 MHz, $CDCl_3$): δ 8.03-7.89 (m, 2H), 7.71 (s, 1H), 7.58-7.40 (m, 4H), 7.32 (d, *J* 8.1 Hz, 2H), 6.83 (s, 1H), 6.76 (dd, *J* 7.9 and 1.2 Hz, 2H), 4.87 and 4.63 (AB system, 2H), 3.27 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.3, 145.7, 143.7, 142.6, 140.3, 136.5, 134.9, 134.3, 131.9, 131.0, 130.52, q 129.76, 128.3, 126.2, 125.8, 100.4, 91.1, 83.8, 73.8, 56.1, 21.47.

***(R,S_S)*-1-(3-(4-Chlorophenyl)-1-(methoxymethoxy)prop-2-ynyl)-2-(*p*-tolylsulfinyl)benzene 3c**. The product was obtained as single diastereomer following the standard procedure from **1a** (200 mg, 0.69 mmol) and sulfone **2c**[20] and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 1:9 as eluent. Colorless oil (131 mg, 45% yield, d.r. 98:2).

$[\alpha]_D^{20}$ -170.0 (*c* 2.7, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.07 (t *J* 1.8 Hz, 1H), 8.02-7.95 (m, 3H), 7.76-7.68 (m, 2H), 7.32 (d, *J* 8.1 Hz, 2H), 7.19 (d, *J* 4 Hz, 4H) 6.00 (s, 1H), 5.08 and 4.68 (AB system, 2H), 3.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 142.1, 141.3, 133.0, 131.5, 130.0, 129.9, 129.8, 128.6, 128.2, 125.8, 125.7, 125.4, 124.1, 120.5, 100.2, 94.0, 86.9, 63.7, 56.2, 23.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{24}H_{22}ClO_3S$ 425.0978; Found 425.0979.

***(R,S$_S$)*-1-(1-(Methoxymethoxy)-3-(4-methoxyphenyl)prop-2-ynyl)-2-(*p*-tolylsulfinyl)benzene 3d**. The product was obtained as single diastereomer following the standard procedure from **1a** (235 mg, 0.81 mmol) and sulfone **2d**[19] and was purified by flash column chromatography using a mixture of EtOAc/hexane 1:9 as eluent. White solid (232 mg, 68% yield, d.r. 96:4).

$[\alpha]_D^{20}$ -196.0 (*c* 2.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02-7.93 (m, 1H), 7.76-7.70 (m, 1H), 7.62-7.46 (m, 4H), 7.26 (dd, *J* 7.9 and 6.2 Hz, 2H), 7.18 (d, *J* 8.0 Hz, 2H), 6.80 (dd, *J* 9.3 and 2.3 Hz, 2H), 6.03 (s, 1H), 5.09 and 4.68 (AB system, 2H), 3.79 (s, 3H), 3.46 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.9, 143.6, 142.2, 141.3, 137.3, 133.3, 131.5, 129.9, 129.8, 128.2, 125.7, 125.4, 125.2, 113.8, 93.9, 88.2, 84.5, 63.8, 56.2, 55.3, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{25}H_{25}O_4S$ 421.1473; Found 421.1469.

***(R,S$_S$)*-3-(3-(Methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)prop-1-ynyl)thiophene 3e.** The product was obtained as single diastereomer following the standard procedure from **1a** (240 mg, 0.82 mmol)and sulfone **2e**[19] and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 1:9 as eluent. Yellow oil (164 mg, 50% yield, d.r. >98:<2).

$[\alpha]_D^{20}$ -100 (*c* 1.1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.02 – 7.96 (m, 1H), 7.76 – 7.71 (m, 1H), 7.61 – 7.48 (m, 4H), 7.38 (dd, *J* 3.0 and 1.2 Hz, 1H), 7.29 – 7.16 (m, 3H), 7.01 (dd, *J* 5.0 and 1.2 Hz, 1H), 6.03 (s, 1H), 5.08 and 4.68 (AB system, 2H), 3.46 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 142.1, 141.3, 137.0, 131.5, 129.9, 129.7, 129.6, 128.1, 125.6, 125.3, 94.0, 85.5, 83.3, 63.7, 56.2, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{22}H_{21}O_3S_2$ 397.0932; Found 397.09468.

***(R,S$_S$)*-2-(3-(Methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)prop-1-ynyl)naphthalene 3f**. The product was obtained as single diastereomer following the standard procedure from **1a** (200 mg, 0.69 mmol)and sulfone **2f**[21] and was purified by crystallization from hexane-CH_2Cl_2. White solid (162 mg, 60% yield, d.r. 97:3).

$[\alpha]_D^{20}$ -208.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07-7.98 (m, 1H), 7.84 (s, 1H), 7.82-7.70 (m, 4H), 7.63-7.53 (m, 4H), 7.48 (dq, *J* 7.5 and 4.2 Hz, 2H), 7.35 (dd, *J* = 8.3 and 1.7 Hz, 1H), 7.18 (d, *J* 7.9 Hz, 2H), 6.09 (s, 1H), 5.13 and 4.72 (AB system, 2H), 3.48 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 142.2, 141.4, 137.1, 133.0, 132.8, 131.9, 131.6, 129.9, 128.2, 127.9, 127.7, 126.9, 126.6, 125.8, 125.2, 119.2, 94.1, 88.4, 86.1, 63.7, 56.3, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{28}H_{25}O_3S$ 441.1524; Found 441.1524.

***(R,S$_S$)*-Triisopropyl(3-(methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)prop-1-ynyl)silane 3h**. The product was obtained as single diastereomer following the standard procedure from **1a** (220 mg, 0.75 mmol)and sulfone **2h**[22] and was purified by flash column chromatography using a mixture of EtOAc/hexane 1:9 as eluent. Yellow oil (232 mg, 65% yield, d.r. >98:<2).

$[\alpha]_D^{20}$ -233.7 (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98-7.89 (m, 1H), 7.78-7.68 (m, 1H), 7.57-7.45 (m, 4H), 7.26-7.15 (m, 2H), 5.87 (s, 1H), 5.10 and 4.65 (AB system, 2H), 3.44 (s, 3H), 2.33 (s, 3H), 1.01-0.98 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.5, 142.4, 141.4, 137.0, 131.5, 130.1, 128.8, 125.5, 124.8, 103.6, 93.9, 90.0, 63.4, 56.3, 21.4, 18.6, 11.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{27}H_{39}O_3SSi$ 471.2311; Found 471.2300.

General Procedure for the Quaternization of Sulfoxides 3.

To a stirred solution of the protected alcohol **3** (50 mg, 0.23 mmol, 1 equiv) and 18-crown-6 ether (1.3 equiv, when was necessary) in THF (6 mL) at -78 ºC under argon atmosphere, KHMDS (1 M in THF) (280 µL, 1.2 equiv) was added. After 10 min a solution of alkyl bromide **4** (0.3 mmol, 1.4 equiv) in THF (2 mL) was added. When the reaction was complete (TLC), a saturated aqueous NH_4Cl was added and the mixture was extracted with CH_2Cl_2. The organic phase was dried (Na_2SO_4) and evaporated under vacuum. The residue was purified by flash column chromatography using a mixture of EtOAc/hexane as eluent.

***(S,S$_S$)*-(3-(Methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)but-1-yne-1,4-diyl)dibenzene 5a/5a´**. The product was obtained as 80:20 diastereomeric mixture following the standard procedure from **3a** and benzyl bromide **4a** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Yellow oil (46 mg, 56% yield) $[\alpha]_D^{20}$ -211 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.20 (dd, *J* 8.4 and 1.3 Hz, 1H), 7.64 (d, *J* 7.0 Hz, 1H), 7.60-7.47 (m, 2H), 7.46-7.25 (m, 6H), 7.25-7.13 (m, 6H), 7.07-6.96 (m, 2H), 5.08 and 5.02 (AB system, 2H), 3.37 (s, 3H), 3.06 and 2.85 (AB system, 2H), 2,32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.8, 143.7, 140.62, 140.00, 135.2, 131.6, 131.0, 129.9, 129.6, 129.3, 129.0, 128.6, 128,4, 127.5, 126.9, 126.7, 126.3, 121.9, 93.3, 92.31, 86.7, 82.8, 55.4, 49.4, 21.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{31}H_{29}O_3S$ 481.1837; Found 481.1827.

Minor diastereomer: Yellow oil (11 mg, 14% yield); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.24 (dd, J = 8.2 and 1.4 Hz, 1H), 7.62-7.53 (m, 2H), 7.52-7.44 (m, 3H), 7.41-7.30 (m, 4H), 7.27-7.18 (m, 3H), 7.17-7.07 (m, 3H), 7.03-6.95 (m, 2H), 5.30 and 4.40 (AB system, 2H), 3.76 and 3.69 (AB system, 2H), 3.35 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.6, 143.5, 141.42, 140.00, 136.9, 131.6, 131.4, 129.2, 129.1, 129.0, 128.9, 128.6, 128,3, 127.4, 126.8, 126.6, 126.2, 122.0, 93.5, 93.0, 86.5, 82.6, 55.2, 49.2, 21.1.

***(S,S$_S$)*-1-(2-(Methoxymethoxy)-1-(3-methoxyphenyl)-4-phenylbut-3-yn-2-yl)-2-(*p*-tolylsulfinyl) benzene 5b/5b´**. The

product was obtained as 80:20 diastereomeric mixture following the standard procedure from **3a** and 3-methoxybenzyl bromide **4b** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Yellow oil (44 mg, 68% yield), $[\alpha]_D^{20}$ -261 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.20 (dd, *J* 8.1 and 1.6 Hz, 1H), 7.60 -7.49 (m, 4H), 7.41-7.33 (m, 1H), 7.32 - 7.16 (m, 8H), 7.08 (q, *J* 7.3 and 6.7 Hz, 1H), 6.79-6.72 (m, 1H), 6.61 (d, *J* 7.5 Hz, 1H), 6.53 (dd, *J* 2.7 and 1.5 Hz, 1H), 5.11 and 5.04 (AB system, 2H), 3.65 (s, 3H), 3.40 (s, 3H), 3.05 and 2.83 (AB system, 2H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.8, 143.3, 142.9, 141.3, 141.0, 136.9, 131.5, 130.3, 129.7, 129.1, 128.8, 128.7, 128.3, 128.3, 127.1, 126.7, 123.6, 121.9, 116.5, 112.8, 94.1, 91.2, 88.2, 80.6, 56.6, 55.0, 50.1, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{32}H_{31}O_4S$ 511.1943; Found 511.1941.

***(S,S_S)*-4-(2-(Methoxymethoxy)-4-phenyl-2-(2-(*p*-tolylsulfinyl)phenyl)but-3-ynyl)benzonitrile 5c/5c´**. The product was obtained as 86:14 diasteromeric mixture following the standard procedure from **3a** and 4-(bromomethyl)benzonitrile **4c** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Yellow oil (46 mg, 71% yield), $[\alpha]_D^{20}$ -272 (*c*, 2.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.16 (dd, *J* 8.2 and 1.4 Hz, 1H), 7.60-7.45 (m, 7H), 7.41 (td, *J* 7.4 and 1.4 Hz, 1H), 7.35-7.29 (m, 1H), 7.29-7.14 (m, 7H), 5.08 and 5.02 (AB system, 2H), 3.36 (s, 3H), 3.15 and 3.00 (AB system, 2H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.1, 142.9, 141.4, 141.1, 140.7, 131.9, 131.4, 131.2, 130.7, 129.7, 129.5, 129.1, 128.4, 128.0, 127.3, 126.9, 121.4, 118.9, 110.7, 94.2, 91.8, 87.6, 79.7, 56.7, 50.2, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{32}H_{28}NO_3S$ 506.1789; Found 506.1786.

***(S,S_S)*-1-(2-(Methoxymethoxy)-4-(4-methoxyphenyl)-1-phenylbut-3-yn-2-yl)-2-(*p*-tolylsulfinyl)benzene 5d/5d´**. The product was obtained as 70:30 diastereomeric mixture following the standard procedure from **3d** and benzyl bromide **4a** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Yellow oil (30 mg, 50% yield), $[\alpha]_D^{20}$ -289 (*c*, 0.68, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.20 (dd, *J* 8.0 and 1.4 Hz, 1H), 7.61-7.53 (m, 2H), 7.52-7.39 (m, 3H), 7.35 (dd, *J* 7.9 and 1.4 Hz, 1H), 7.28-7.17 (m, 3H), 7.16-7.06 (m, 3H), 6.98 (dd, *J* 7.5 and 2.0 Hz, 2H), 6.92-6.84 (m, 2H), 5.31 and 4.40 (AB system, 2H) 3.83 (s, 3H), 3.78 and 3.69 (AB system, 2H), 3.35 (s, 3H), 2.36 (s, 3H); ^{13}C NMR(75 MHz, $CDCl_3$): δ 158.7, 143.2, 142.9, 141.3, 141.0, 136.9, 131.5, 130.3, 129.7, 129.1, 128.8, 128.7, 128.3, 128.3, 127.1, 126.7, 123.6, 121.9, 116.5, 112.8, 94.1, 91.2, 88.2, 80.6, 56.6, 55.0, 50.1, 21.4. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{32}H_{31}O_4S$ 511.1943; Found 511.1935.

***(S,S_S)*-Triisopropyl(3-(methoxymethoxy)-4-(3-methoxyphenyl)-3-(2-(*p*-tolylsulfinyl)phenyl)but-1-ynyl)silane 5e**. The product was obtained as >98:2 diastereomeric mixture following the standard procedure from **3h** and 3-methoxybenzyl bromide **4e** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Colorless oil (32 mg, 51% yield), $[\alpha]_D^{20}$ -140 (*c*, 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.25 (dd, *J* 7.9 and 1.4 Hz, 1H), 7.57 (dd, *J* 7.2 and 5.5 Hz, 2H), 7.54-7.45 (m, 2H), 7.33 (t, *J* 7.8 Hz, 1H), 7.29-7.20 (m, 2H), 7.04 (t, *J* 7.9, 1H), 6.73-6.68 (m, 1H), 6.59 (d, *J* 7.4 Hz, 1H), 6.37-6.29 (m, 1H), 5.12 and 5.00 (AB system, 2H), 3.64 (s, 3H), 3.40 (s, 3H), 2.87 and 2.56 (AB system, 2H), 2.35 (s, 3H), 1.09-1.02 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.7, 143.4, 142.8, 141.5, 140.9, 136.9, 130.0, 129.8, 129.3, 128.9, 128.3, 127.2, 126.4, 123.6, 116.8, 112.2, 105.0, 94.1, 93.2, 81.4, 56.6, 55.0, 49.9, 21.4, 18.5, 11.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{35}H_{47}O_4SSi$ 591.2964; Found 591.2956.

***(S,S_S)*-1-(3-(Methoxymethoxy)-1-phenylhepta-1,5-diyn-3-yl)-2-(*p*-tolylsulfinyl)benzene 5f/5f´**. The product was obtained as an inseparable 55:45 diasteromeric mixture (29 mg, 52% yield) following the standard procedure from **3a** and 1-bromo-2-butyne **4f** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Diastereomeric mixture (55:45): Yellow oil, $[\alpha]_D^{20}$ -120 (*c*, 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.13 (dd, *J* 7.6 and 1.8 Hz, 1H), 8.02-7.94 (m, 1H), 7.92-7.87 (m, 1H), 7.84-7.77 (m, 1H), 7.63-7.42 (m, 13H), 7.39-7.25 (m, 6H), 7.25-7.13 (m, 4H), 5.45 and 4.89 (AB system, 2H), 5.38 and 4.59 (AB system, 2H), 3.47 (s, 3H), 3.46 (s, 2H), 3.43-3.32 (m, 1H), 3.21-2.98 (m, 3H), 2.34 (d, J 5.1 Hz, 6H), 1.75 (bs, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.0, 144.6, 143.9, 140.7, 140.5, 140.3, 132.0, 132.0, 130.5, 130.3, 129.7, 129.6, 129.6, 129.5, 129.1, 129.0, 128.5, 128.4, 127.9, 127.7, 127.2, 126.7, 126.1, 126.0, 125.1, 121.9, 93.6, 93.4, 90.7, 90.5, 87.5, 87.2, 80.8, 80.2, 79.6, 78.0, 74.2, 74.0, 57.0, 56.8, 35.3, 33.8, 21.4, 21.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{28}H_{27}O_3S$ 443.1680; Found 443.1681.

***(S,S_S)*-1-(3-(Methoxymethoxy)-1-phenylhex-5-en-1-yn-3-yl)-2-(*p*-tolylsulfinyl)benzene 5g/5g´**. The product was obtained as an inseparable 70:30 diasteromeric mixture (35 mg, 64% yield) following the standard procedure from **3a** and allyl bromide **4g** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Diastereomeric mixture (70:30): Yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 8.23-8.05 (m, 2H), 7.73 (dd, *J* 7.3 and 1.8 Hz, 1H), 7.61-7.37 (m, 12H), 7.35-7.11 (m, 8H), 5.89-5.66 (m, 1H), 5.27-5.20 (d, *J* 6 Hz, 1H), 5.10-4.85 (m, 2H), 4.74-4.63 (d, *J* 5 Hz, 1H), 3.53-3.39 (m, 3H), 2.35 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.0, 143.6, 143.9, 140.7, 140.5, 140.3, 132.0, 132.0, 130.5, 130.3, 129.7, 129.6, 129.6, 129.5, 129.1, 129.0, 128.5, 128.4, 127.9, 127.7, 127.2, 126.7, 126.1, 126.0, 125.1,

121.9, 93.6, 93.4, 90.7, 90.5, 80.8, 80.2, 79.6, 78.0, 74.2, 74.0, 57.0, 56.8, 48.8, 48. 6, 35.3, 33.8, 21.4, 21.3; HRMS (ESI-TOF) m/z: ([M+H]$^+$ Calcd. for $C_{27}H_{27}O_3S$ 431.1680; Found 431.1681.

***(S,S$_S$)*-1-(2-(Methoxymethoxy)-4-phenylbut-3-yn-2-yl)-2-(*p*-tolylsulfinyl)benzene 5h/5h´**. The product was obtained as 80:20 diastereomeric mixture following the standard procedure, without 18-crown-6 ether, from **3a** and methyl iodide and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Colorless oil (29 mg, 56% yield), $[\alpha]_D^{20}$ -220 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00-7.95 (m, 1H), 7.67-7.62 (m, 1H), 7.57-7.50 (m, 2H), 7.49-7.41 (m, 4H), 7.38-7.23 (m, 6H), 7.22-7.14 (m, 3H), 5.43 and 4.79 (AB system, 2H), 3.40 (s, 3H), 2.34 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.2, 144.0, 142.8, 140.4, 132.0, 130.8, 129.6, 128.9, 128.4, 128.3, 128.0, 126.0, 125.5, 122.1, 94.5, 93.3, 89.1, 75,4, 56.2, 29.7, 21.4; HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd. for $C_{25}H_{25}O_3S$ 405.1524; Found 405.1525.

***(S,S$_S$)*-Triisopropyl-3-(methoxymethoxy)-3-(2-(*p*-tolylsulfinyl)phenyl)hepta-1,5-diyn-1-yl)silane 5i/5i´**. The product was obtained as 91:9 diastereomeric mixture following the standard procedure with 18-crown-6 ether, from **3h** and 1-bromo-2-butyne **4f** and was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 15:85 as eluent.

Major diastereomer: Colorless oil (36 mg, 66% yield), $[\alpha]_D^{20}$ -63.81 (*c* 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.91 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.56 – 7.39 (m, 4H), 7.18 (d, *J* = 7.9 Hz, 2H), 5.35 and 4.44 (AB system, 2H), 3.40 (s, 3H), 3.27 (dq, *J* = 16.4, 2.4 Hz, 1H), 3.13 (dq, *J* = 16.1, 2.4 Hz, 1H), 2.33 (s, 3H), 1.74 – 1.63 (m, 4H), 1.12 (s, 21H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.5, 144.2, 140.1, 139.9, 129.9, 129.4, 129.3, 128.1, 126.3, 125.9, 104.5, 93.1, 92.6, 81.2, 79.7, 73.9, 56.7, 35.4, 21.2, 18.5, 11.1. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd. for $C_{31}H_{43}O_3SSi$ 523.2702; Found 523.2698.

General Procedures for the Cleavage of MOM Group of 3.

Method A.[14a] To a stirred solution of **3** (80 mg, 0.2 mmol, 1 equiv) in CH_2Cl_2 (5 mL) cooled at 0 ºC $ZnBr_2$ (66 mg, 0.3 mmol, 1.5 equiv) and *n*-PrSH (53 µL, 0.6 mmol, 3 equiv) were added. The mixture was stirred at 0 ºC for 20 min and at room temperature until the reaction was completed (TLC). The mixture was diluted with CH_2Cl_2 (10 mL) and a saturated solution of $NaHCO_3$ (5 mL) was added. The organic layer was washed with brine, dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by flash column chromatography using a mixture of EtOAc/hexane as eluent.

Method B.[14b] To a stirred solution of **3** (40 mg, 0.2 mmol, 1 equiv) and 2,2'-bipyridyl (468 mg, 0.3 mmol, 3 equiv) in CH_2Cl_2 (5 mL) cooled at 0 ºC under argon atmosphere TMSOTf (363 µL, 0.2 mmol, 2 equiv) were added. The mixture was stirred at 0 ºC for 30 min and at room temperature until the reaction was completed (TLC). Then, the mixture was diluted with water (5 mL) and CH_2Cl_2 (5 mL) until the pyridinium salt disappeard (TLC). The mixture was extracted with CH_2Cl_2, dried (Na_2SO_4) and the solvent was evaporated. The residue was purified by flash column chromatography using a mixture of EtOAc/hexane as eluent.

***(R,S$_S$)*-3-Phenyl-1-(2-(*p*-tolylsulfinyl)phenyl)prop-2-yn-1-ol 6a**. The product was obtained following the general procedure A or B from **3a** and was purified by flash column chromatography using a mixture of EtOAc/hexane 2:8 as eluent. The product is a white solid (46 mg, 65% yield by method A and 25 mg, 70% by method B).

Prepared through method A. $[\alpha]_D^{20}$ -175 (*c* 0.5, acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.83-7.80 (dd, *J* 7.5 and 1.5 Hz, 1H), 7.73 (dd, *J* 7.8 and 1.5 Hz, 1H), 7.54 (d, *J* 8.1 Hz, 2H), 7.43 (dtd, *J* 21.6, 7.4 and 1.5 Hz, 2H), 7.34-7.21 (m, 5H), 7.16 (d, *J* 8.0, 2H), 6.07 (bs, 1H), 3.45 (bs, 1H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.4, 141.2, 141.1, 139.9, 131.8, 131.6, 130.1, 129.5, 128.7, 128.3, 128.0, 126.1, 125.5, 122.3, 88.1, 87.2, 61.3, 21.4. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd. for $C_{22}H_{18}O_2S$ 346.1028; Found 346.1035.

***(R,S$_S$)*-3-(Naphthalen-2-yl)-1-(2-(*p*-tolylsulfinyl)phenyl) prop-2-yn-1-ol 6b**. The product was obtained following the general procedure A from **3h** and was purified by flash column chromatography using a mixture of EtOAc/hexane 2:8 as eluent. The product is a white solid (39 mg, 58% yield), mp 125-127 ºC.

Prepared through method A. $[\alpha]_D^{20}$ -170 (*c* 0.6, acetone); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 – 7.69 (m, 7H), 7.64 – 7.43 (m, 7H), 7.37 (dd, *J* 8.5 and 1.6 Hz, 1H), 7.18 (dd, *J* 8.3 and 3.0 Hz, 2H), 6.15 (d, *J* 3.8 Hz, 1H), 4.68 (s, 1H), 3.50 (bs, 1H), 2.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 142.6, 141.7, 141.1, 139.7, 132.9, 132.7, 131.8, 131.6, 130.0, 129.5, 128.2, 127.9, 127.8, 127.7, 126.8, 126.6, 126.1, 126.0, 125.7, 119.3, 88.1, 87.7, 61.5, 21.3; HRMS (ESI-TOF) m/z: [M–H_2O] Calcd. for $C_{26}H_{19}OS$ 379.1157; Found 379.1158.

General Procedure for the Desulfinylation of Sulfoxides 5.

To a stirred solution of sulfoxide **5** (0.106 mmol, 1 equiv) in THF (10 mL) cooled at -78º C under argon atmosphere a 1.7M solution of *t*-BuLi (0.425 mmol, 4 equiv) was added and the mixture was stirred at this temperature for 15 min. When the reaction was complete (TLC), a saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The organic phase was dried (Na_2SO_4) and evaporated. The residue was purified by preparative thin layer chromatography using a mixture of EtOAc/hexane 5:95 as eluent.

(*R*)-(2-(Methoxymethoxy)but-3-yne-1,2,4-triyl)tribenzene 7a. The product was obtained (33 mg, 90% yield) following the standard procedure from **5a**.

Colorless oil, $[\alpha]_D^{20}$ -36 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.58 (dt, *J* 7.6 and 1.7 Hz, 2H), 7.47 – 7.39 (m, 2H), 7.32 (dd, *J* 6.2 and 2.3 Hz, 6H), 7.18 (dd, *J* 4.5 and 2.0 Hz, 3H), 7.09 (dq, *J* 5.1 and 1.9 Hz, 2H), 4.88 and 4.79 (AB system, 2H), 3.46 and 3.19 (AB system, 2H), 3.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 136.0, 131.6, 131.1, 128.6, 128.3, 128.0, 127.9, 127.3, 126.7, 126.5, 122.5, 93.6, 90.2, 87.94, 79.6, 56.3, 51.59; HRMS (ESI-TOF) m/z: $[M+(NH4^+)]$ Calcd. for $C_{24}H_{26}NO_2$ 360.1963; Found 360.1971.

(*R*)-(3-(Methoxymethoxy)but-1-yne-1,3-diyl)dibenzene 7b. The product was obtained (36 mg, 85% yield) following the standard procedure from **5h**.

Colorless oil, $[\alpha]_D^{20}$ -35 (*c* 0.64, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.76 – 7.67 (m, 2H), 7.52 (dd, *J* 6.9 and 3.2 Hz, 2H), 7.35 (qt, *J* 7.7 and 4.2 Hz, 6H), 4.97 (dd, *J* 6.3 and 1.8 Hz, 1H), 4.77 (dd, *J* 6.4 and 1.8 Hz, 1H), 3.42 (s, 3H), 1.89 (s, 3H); ^{13}C RMN (75 MHz, $CDCl_3$) δ 143.6, 140.7, 131.7, 130.7, 129.5, 128.9, 128.6, 122.1, 92.3, 85.5, 70.4, 32.1.

General Procedures for the Cleavage of MOM Group of 5.

These compounds were prepared following the general procedures A or B for the cleavage of MOM group described previously.

***(S,Ss)*-1,4-Diphenyl-2-(2-(*p*-tolylsulfinyl)phenyl)but-3-yn-2-ol 8a**. The product was obtained following the general procedure A or B from **5a** (50 mg, 0.104 mmol)and was purified by flash column chromatography using a mixture of EtOAc/hexane 2:8 as eluent (27 mg, 60% yield by method A and 23 mg, 50% by method B).

Prepared through method A. White solid, $[\alpha]_D^{20}$ -227 (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.29 (dd, *J* 7.9 and 1.4 Hz, 1H), 7.73 (dd, *J* 7.8 and 1.4 Hz, 1H), 7.63 and 7.18 (AA'BB' system, 4H), 7.54 (td, *J* 7.6 and 1.4 Hz, 1H), 7.42 (dd, *J* 7.5 and 2.0 Hz, 3H), 7.32 (tt, *J* 6.3 and 4.6 Hz, 8H), 3.64 and 3.39 (AB system, 2H), 2.85 (bs, 1H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.2, 144.1, 141.6, 140.7, 135.1, 131.7, 131.2, 130.5, 129.7, 129.5, 128.9, 128.5, 128.2, 127.8, 127.5, 126.5, 126.3, 122.0, 90.1, 88.8, 75.7, 51.1, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{29}H_{25}O_2S$ 437.1570; Found 437.1580.

***(S,Ss)*-4-Phenyl-2-(2-(*p*-tolylsulfinyl)phenyl)but-3-yn-2-ol 8b**. The product was obtained following the general procedure A or B from **5h** (50 mg, 0.123 mmol)and was purified by flash column chromatography using a mixture of EtOAc/hexane 2:8 as eluent (29 mg, 65% yield by method A and 31 mg, 71% by method B).

Prepared through method A. White solid, $[\alpha]_D^{20}$ -226 (*c* 0.42, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.09 – 8.03 (m, 1H), 7.70 (dt, *J* 5.5 Hz and 3.5, 1H) 7.53 and 7.16 (AA'BB' system, 4H), 7.47 – 7.34 (m, 4H), 7.41 – 7.36 (m, 2H), 7.31 – 7.24 (m, 3H), 3.30 (s, 1H), 2.32 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.7, 143.6, 143.2, 140.7, 131.7, 130.7, 129.5, 128.9, 128.6, 128.2, 126.8, 126.4, 126.2, 122.1, 92.8, 85.5, 70.6, 32.4, 21.3. HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd. for $C_{23}H_{21}O_2S$ 361.1262; Found 361.1254.

(*R*)-1,2,4-Triphenylbut-3-yn-2-ol 9a. The product was obtained from **8a** (19 mg, 60% yield) following the general procedure for the desulfinylation reactions described previously.

Colorless oil, $[\alpha]_D^{20}$ +2.05 (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.70 - 7.68 (m, 1H), 7.67 - 7.65 (m, 1H), 7.45 – 7.39 (m, 3H), 7.39 – 7.37 (m, 1H), 7.36 – 7.30 (m, 4H), 7.28 (dd, *J* = 2.8, 2.0 Hz, 4H), 3.25 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.15, 135.90, 131.65, 131.01, 128.53, 128.29, 128.14, 127.88, 127.77, 127.03, 125.63, 91.0, 87.35, 73.64, 51.98. HRMS (ESI-TOF) m/z: $[M-H_2O]$ Calcd. for $C_{22}H_{17}$ 281.1330; Found 281.1331.

***(R)*-2,4-Diphenylbut-3-yn-2-ol 9b**. The product was obtained from **8b** (26 mg, 84% yield) following the general procedure for the desulfinylation reactions described previously.

Colorless oil, *ee* 97% by HPLC, $[\alpha]_D$ -8.25 [0.4, $CHCl_3$], (lit.[6a] $[\alpha]_D$ +5.2 [2.5, $CHCl_3$] *ee* 61% for the (*S*) isomer; lit.[6b] $[\alpha]_D$ -4.0 [1.85, $CHCl_3$] *ee* 53%; lit.[6c] $[\alpha]_D$ -6.0 [0.66, $CHCl_3$] *ee* 86%); ^1H NMR (300 MHz, $CDCl_3$): δ 7.74 (dd, *J* 7.5 and 2.0 Hz, 2H), 7.49 (dt, *J* 7.2 and 3.4 Hz, 2H), 7.44 – 7.28 (m, 6H), 2.45 (bs, 1H), 1.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 145.8, 131.8, 128.6, 128.6, 128.4, 128.0, 125.2, 122.8, 92.6, 85.2, 70.6, 33.4. HPLC condition: CHIRALCEL OJ 250 x 4.6 mm 10 µm, 10% isopropanol in hexane, 1.0 mL/min. T_R = 15.13 (major).

Supporting Information Available. The Supporting Information is available free of charge on the ACS Publication website at DOI: 10.1021/acs.joc.7b01211. Copies of ^1H and ^{13}C spectra for all new compounds and X-ray data for compound **6a** are included. This material is free of charge via the Internet at http://pubs.acs.org.

Corresponding Authors
*E-MAIL: (FY) yustef@unam.mx; (JA) jose.aleman@uam.es, www.uam.es/jose.aleman

ACKNOWLEDGMENTS

We thank DGAPA-UNAM (project number PAPIIT-IN205316) for financial support. R. I. Rodríguez thanks CONACYT for a graduated fellowship (grant number 605795) and E. Ramírez thanks DGAPA-UNAM for a

posdoctoral fellowship and Prof. J. M. Muchowski for reviewing the manuscript. We also thank E. García Ríos, C. García González, R. Gaviño, L. C. Márquez, M. A. Peña and L. M. Ríos for their technical assistance. Financial support from the Spanish Government (CTQ2015-64561-R) is also gratefully acknowledged.

REFERENCES

(1) (a) Corey, E. J.; Guzmán-Pérez A. *Angew. Chem. Int. Ed*. **1998**, *37*, 388. (b) Christoffers J.; Mann A. *Angew. Chem. Int. Ed.* **2001**, *40*, 4591. (c) Modern Acetylene Chemistry, (Eds. P. J. Stang, F. Diederich), VCH, Weinheim, 1995.

(2) For a [2+2+2] process, see: Witulski, B.; Zimmermann, A.; Gowans, N. D. *Chem. Commun*. **2002**, 2984. For a review on hydrometallations, see: Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, 853.

(3) For some representative examples in the synthesis of natural products, see: (a) Roethle, P. A.; Trauner, D. *Org. Lett*. **2006**, *8*, 345. (b) Trost, B. M.; Mueller, T. J. J.; Martinez, J. *J. Am. Chem. Soc.* **1995**, *117*, 1888. (c) Zhu, G.; Lu, X. *J. Org. Chem.* **1995**, *60*, 1087. (d) Fleming, J. J.; Du Bois, J. *J. Am. Chem. Soc.* **2006**, *128*, 3926. (e) Yoon, T.; Shair, M. D.; Danishefsky, S. J.; Shulte, G. K. *J. Org. Chem*. **1994**, *59*, 3752.

(4) (a) DiMauro, E. F.; Kozlowski M. C. *J. Am. Chem. Soc*. **2002**, *124*, 12668. (b) Jeon, S.-J.; Li, H.; García, C., LaRochelle, L. K.; Walsh, P. J. *J. Org. Chem*. **2005**, *70*, 448.

(5) For reviews, see: (a) Cozzi, P. G.; Hilgraf, R.; Zimmermann, N. *Eur. J. Org. Chem*. **2004**, 4095. (b) Pu, L. *Tetrahedron* **2003**, *59*, 9873. (c) Pu, L.; Yu, H.-B. *Chem. Rev*. **2001**, *101*, 757. (d) Soai, K.; Niwa, S. *Chem. Rev*. **1992**, *92*, 833. (e) Lu, G.; Li, Y. M.; Li, X. S.; Chan, A. S. C. *Coord. Chem. Rev.* **2005**, *249*, 1736. (f) Trost, B. M.; Weiss A. H. *Adv. Synth. Catal*. **2009**, *351*, 963.

(6) See for example: (a) Cozzi, P. G. *Angew. Chem. Int. Ed*. **2003**, *42*, 2895. (b) Forrat, V. J.; Prieto, O.; Ramón, D. J.; Yus, M. *Chem. Eur. J.* **2006**, *12*, 4431. (c) Liu, L.; Wang, R.; Kang, Y.-F.; Chen, C.; Xu, Z.-Q.; Zhou, Y.-F.; Ni, M.; Cai, H.-Q.; Gong, M.-Z. *J. Org. Chem*. **2005**, *70*, 1084.

(7) Constable, D. J. C.; Dunn, P. J., Hayler, J. D.; Humphrey, G. R.; Leazer Jr., J. L.; Linderman, R. J.; Lorenz, K.; Manley, J.; Pearlman, B. A.; Wells, A.; Zaks, A.; Zhang, T. Y. *Green Chem*. **2007**, *9*, 411.

(8) (a) García Ruano, J. L.; Alemán, J.; Marzo, L.; Alvarado, C.; Tortosa, M.; Díaz-Tendero, S.; Fraile, A. *Angew. Chem. Int. Ed*. **2012**, *51*, 2712. (b) García Ruano, J. L.; Alemán, J.; Marzo, L.; Alvarado, C.; Tortosa, M.; Díaz-Tendero, S.; Fraile, A. *Chem. Eur. J.* **2012**, *18*, 8414. (c) García Ruano, J. L.; Marzo, L.; Alvarado, C.; Marcos, V.; Alemán J.; *Chem. Eur. J.* **2012**, *18*, 9775. (d) Pérez, I.; Yuste, F.; Sánchez-Obregón, R.; Toscano, R. A.; Alemán, J.; Marzo, L.; Martín Castro, A. M.; Alonso, I.; García Ruano, J. L. *Eur. J. Org. Chem*. **2015**, 3314. (e) Esteban, F.; Boughani, L.; García Ruano, J. L.; Fraile, A.; Alemán, J. *Org. Biomol. Chem*. **2017**, *15*, 3901. (f) Valderas, C.; Marzo, L.; de la Torre, M. C.; García Ruano, J. L.; Alemán, J.; Casarrubios, L.; Sierra, M. A. *Chem. Eur. J*, **2016**, *24*, 15645. (g) Marzo, L.; Pérez, I.; Yuste, F.; Alemán, J.; García Ruano, J. L. *Chem. Commun*. **2015**, *51*, 346.

(9) (a) García Ruano, J. L.; Alemán, J.; Parra, A. *J. Am. Chem. Soc.* **2005**, *127*, 13048. (b) García Ruano, J. L.; Alemán, J.; Catalán, S.; Marcos, V.; Monteagudo, S.; Parra, A.; del Pozo, C.; Fustero, S. *Angew. Chem. Int. Ed*. **2008**, *47*, 7941; (c) Arroyo, Y.; Meana, A.; Sanz-Tejedor, M. A.; Alonso, I.; García Ruano, J. L. *Chem. Eur. J*. **2010**, *16*, 9874.

(10) The carbanion derived form **1** exhibits a purples color which indicates the formation of the anion.

(11) The reaction of the alkylsulfone was additionally performed under the same conditions (LDA, -78 ºC, 1 h) without the presence of the sulfinylbenzyl derivative. We found the formation of the corresponding allenylsulfone, which would be the possible reason for null reactivity of sulfinylcarbanion to give the anti-Michael type product.

(12) We tried the reaction in one step but all one-pot conditions were unsuccessful.

(13) Greene, T. H.; Wuts, P. G. M. in Protective Groups in Organic Synthesis, Fifth Edition, 2014-Wiley.

(14) (a) Hyun Han, J.; Eun Kwon, Y.; Sohn, J.-H. Hyun Ryu, D. *Tetrahedron*, **2010**, *66*, 1673. (b) Fujioka, H.; Kubo, O.; Senami, K.; Minamitsuji, Y.; Maegawa, T. *Chem Commun*. **2009**, 4429.

(15) CCDC1583023 contains the crystallographic data of **6a** (www.ccdc.cam.ac.uk).

(16) Antczak, M. I.; Cai, F.; Ready, J. M. *Org. Lett*. **2011**, *13*, 184.

(17) (a) García Ruano, J. L.; Martín-Castro, A. M.; Tato, F.; Torrente, E.; Poveda, A. M. *Chem. Eur. J*. **2010**, *16*, 6317. (b) García Ruano, J. L.; Torrente, E.; Martín-Castro, A. M. *J. Org. Chem*. **2011**, *76*, 3597.

(18) Pirkle, W. H.; Hoekstra, M. S. *J. Am. Chem. Soc*. **1976**, *98*, 1832.

(19) Nair, V.; Augustine, A.; Suja, T. D. *Synthesis* **2002**, 2259.

(20) Tang, X.; Dai, C.; Zhu, Q. Chinese patent CN 106565553. Apr 19, 2017, (*CA 166:490267*).

(21) Meesin, J.; Katrun, P.; Paeseecharoen, C.; Pohmakotr, M.; Reutrakul, V.; Soorukram, D.; Kuhakarn, C. *J. Org. Chem*. **2016**, *81*, 2744.

(22) (a) Helal, C. J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938. (b) Kitamura, T.; Kotani, M.; Fujiwara, Y. *Synthesis* **1998**, 1416. (c) Tykwinsky, R.; Williamson, B. L.; Fischer, D. R.; Sang, P. J.; Arif, A. M. *J. Org. Chem*. **1993**, *58*, 5235.